CLAIMS

1. A parenteral vaccine formulation comprising at least one immunogenic substance, and as an adjuvant one or more salts selected from salts formed with a Group 2 element of the Periodic Table selected from Mg, Ca, Sr, Ba and Ra, or a Group 4 element of the Periodic Table selected from Ti, Zr, Hf, and Rf,
and hydrates thereof,
with the proviso that the salt is not calcium phosphate, is not magnesium hydroxide in combination with aluminium hydroxide or aluminium oxide and is not calcium hydroxide in gel combination with zinc hydroxide, lecithin and polyalphaolefine.

2. A parenteral vaccine formulation according to claim 1, wherein the adjuvant is selected from inorganic salts.

3. A parenteral vaccine formulation according to claim 1, wherein the adjuvant is selected from organic salts.

4. A parenteral vaccine formulation according to claims 1-2, wherein the adjuvant is selected from salts formed with oxides, peroxides, hydroxides, carbonates, phosphates, pyrophosphates, hydrogenphosphates, dihydrogenphosphates, sulphates, and/or silicates,
and hydrates thereof.

5. A parenteral vaccine formulation according to claims 1-2, and 4, wherein the adjuvant is selected from salts formed between Mg, Ca, Ba, Ti, or Zr, and oxide, peroxide, hydroxide, and/or carbonate,
and hydrates thereof.

EP 0 925 795 A2

6. A parenteral vaccine formulation according to claims 1-2, and 4-5, wherein the adjuvant is selected from salts formed between

magnesium and oxide, peroxide, hydroxide, and/or carbonate,
calcium and oxide, peroxide, hydroxide, and/or carbonate,
barium and oxide, peroxide, hydroxide, and/or carbonate,
titanium and oxide, peroxide, hydroxide, and/or carbonate, and
zirconium and oxide, peroxide, hydroxide, and/or carbonate,
and hydrates thereof.

7. A parenteral vaccine formulation according to claims 1-2, and 4-6, wherein the adjuvant is selected from magnesium hydroxide, magnesium carbonate hydroxide pentahydrate, titanium dioxide, calcium carbonate, barium hydroxide, barium peroxide, barium carbonate, barium sulphate, beryllium oxide, calcium sulphate, calcium silicate, dicalcium silicate, tricalcium silicate, calcium pyrophosphate, calcium peroxide, calcium hydroxide, tricalcium phosphate, calcium hydrogen-phosphate, calcium dihydrogenphosphate, calcium sulphate dihydrate, magnesium carbonate, magnesium oxide, magnesium dioxide, magnesium sulphate, trimagnesium phosphate, magnesium silicate, dimagnesium trisilicate, magnesium trisilicate, titantium disulphate, zirconium dioxide, zirconium hydroxide, zirconium sulphate, strontium peroxide, and strontium carbonate.

8. A parenteral vaccine formulation according to claims 1-2, and 4-7, wherein the adjuvant is selected from magnesium hydroxide, magnesium carbonate hydroxide pentahydrate, and titanium dioxide.

9. A parenteral vaccine formulation according to claims 1-8 further comprising an additional adjuvant.

10. A parenteral vaccine formulation according to claim 9, wherein the additional adjuvant is selected from saponins such as Quil A and Qs-21, MF59, MPL, PLG, PLGA, calcium phosphate, and aluminium salts.

11. A parenteral vaccine formulation according to claims 1-10 further comprising pharmaceutically acceptable excipients and/or carriers.

12. A parenteral vaccine formulation according to claims 1-11 further comprising diluents, buffers, suspending agents, solubilising agents, pH-adjusting agents, dispersing agents, and/or colorants.

13. A parenteral vaccine formulation according to claims 1-12 for intravenous, intramuscular, intraarticular, subcutaneous, intradermal, epicutantous, and intra-peritoneal administration.

14. A parenteral vaccine formulation according to claims 1-13, wherein the cation of the adjuvant is present in an amount of from about 0.0004 to about 120 M, such as from about 0.004 to about 12 M.

15. A parenteral vaccine formulation according to claim 14, wherein the cation of the adjuvant is present in an amount of from about 0.008 to about 6 M.

16. A parenteral vaccine formulation according to claims 1-15, wherein the adjuvant is magnesium hydroxide.

10503035.052503

17. A parenteral vaccine formulation according to claims 1-15, wherein the adjuvant is magnesium carbonate hydroxide pentahydrate.

18. A parenteral vaccine formulation according to claims 1-15, wherein the adjuvant is titanium dioxide.

19. A parenteral vaccine formulation according to claims 1-15, wherein the adjuvant is a combination of magnesium hydroxide and magnesium carbonate hydroxide pentahydrate, magnesium hydroxide and titanium dioxide, magnesium carbonate hydroxide pentahydrate and titanium dioxide, or magnesium hydroxide, magnesium carbonate hydroxide pentahydrate, and titanium dioxide.

20. A parenteral vaccine formulation according to claims 16-19 further comprising an additional adjuvant selected from saponins such as Quil A and Qs-21, MF59, MPL, PLG, PLGA, calcium phosphate, and aluminium salts.

21. An adjuvant composition for parenteral use comprising one or more salts selected from salts formed with a Group 2 element of the Periodic Table selected from Mg, Ca, Sr, Ba and Ra, or a Group 4 element of the Periodic Table selected from Ti, Zr, Hf, and Rf,
and hydrates thereof,
with the proviso that the salt is not calcium phosphate, is not magnesium hydroxide in combination with aluminium hydroxide or aluminium oxide and is not calcium hydroxide in gel combination with zinc hydroxide, lecithin and polyalphaolefine.

22. An adjuvant composition according to claim 21, wherein the salt is selected from inorganic salts.

23. An adjuvant composition according to claim 21, wherein the salt is selected from organic salts.

24. An adjuvant composition according to claims 21-22, wherein the salt is selected from salts formed with oxides, peroxides, hydroxides, carbonates, phosphates, pyrophosphates, hydrogenphosphates, dihydrogenphosphates, sulphates, and/or silicates,
and hydrates thereof.

25. An adjuvant composition according to claims 21-22, and 24, wherein the salt is selected from salts formed between Mg, Ca, Ba, Ti or Zr, and oxide, peroxide, hydroxide, and/or carbonate,
and hydrates thereof.

26. An adjuvant composition according to claims 21-22, and 24-25, wherein the salt is selected from salts formed between

magnesium and oxide, peroxide, hydroxide, and/or carbonate,
calcium and oxide, peroxide, hydroxide, and/or carbonate,
barium and oxide, peroxide, hydroxide, and/or carbonate,
titanium and oxide, peroxide, hydroxide, and/or carbonate, and
zirconium and oxide, peroxide, hydroxide, and/or carbonate,
and hydrates thereof.

27. An adjuvant composition according to claims 21-22, and 24-26, wherein the salt is selected from magnesium hydroxide, magnesium carbonate hydroxide pentahydrate, titanium dioxide, calcium carbonate, barium hydroxide, barium peroxide, barium carbonate, barium sulphate,

beryllium oxide, calcium sulphate, calcium silicate, dicalcium silicate, tricalcium silicate, calcium pyrophosphate, calcium peroxide, calcium hydroxide, tricalcium phosphate, calcium hydrogenphosphate, calcium dihydrogenphosphate, calcium sulphate dihydrate, magnesium carbonate, magnesium oxide, magnesium dioxide, magnesium sulphate, trimagnesium phosphate, magnesium silicate, dimagnesium trisilicate, magnesium trisilicate, titantium disulphate, zirconium dioxide, zirconium hydroxide, zirconium sulphate, strontium peroxide, and strontium carbonate.

28. An adjuvant composition according to claims 21-22, and 24-27, wherein the salt is selected from magnesium hydroxide, magnesium carbonate hydroxide pentahydrate, and titanium dioxide.

29. An adjuvant composition according to claims 21-28 further comprising an additional adjuvant.

30. An adjuvant composition according to claim 29, wherein the additional adjuvant is selected from saponins such as Quil A and Qs-21, MF59, MPL, PLG, PLGA, calcium phosphate, and aluminium salts.

31. An adjuvant composition according to claims 21-30 further comprising pharmaceutically acceptable excipients and/or carriers.

32. An adjuvant composition according to claims 21-31 further comprising diluents, buffers, suspending agents, solubilising agents, pH-adjusting agents, dispersing agents, and/or colorants.

10505325.050801

33. An adjuvant composition according to claims 21-32, wherein the cation of the salt is present in an amount of from about 0.0004 to about 120 M, such as from about 0.004 to about 12 M.

34. An adjuvant composition according to claim 33, wherein the cation of the salt is present in an amount of from about 0.008 to about 6 M.

35. An adjuvant composition according to claims 21-34, wherein the salt is magnesium hydroxide.

36. An adjuvant composition according to claims 21-34, wherein the salt is magnesium carbonate hydroxide pentahydrate.

37. An adjuvant composition according to claims 21-34, wherein the salt is titanium dioxide.

38. An adjuvant composition according to claims 21-34, wherein the salt is a combination of magnesium hydroxide and magnesium carbonate hydroxide pentahydrate, magnesium hydroxide and titanium dioxide, magnesium carbonate hydroxide pentahydrate and titanium dioxide, or magnesium hydroxide, magnesium carbonate hydroxide pentahydrate, and titanium dioxide.

39. An adjuvant composition according to claims 35-38 further comprising an additional adjuvant selected from saponins such as Quil A and Qs-21, MF59, MPL, PLG, PLGA, calcium phosphate, and aluminium salts.

40. An adjuvant comprising one or more salts selected from salts formed with a Group 2 element of the Periodic Table selected from Mg, Ca, Sr, Ba and Ra, or a Group 4

EP 2 036 569 A2

element of the Periodic Table selected from Ti, Zr, Hf, and Rf,
and hydrates thereof,
with the proviso that the salt is not calcium phosphate, is not magnesium hydroxide in combination with aluminium hydroxide or aluminium oxide and is not calcium hydroxide in gel combination with zinc hydroxide, lecithin and polyalphaolefine.

41. An adjuvant according to claim 40, wherein the salt is selected from inorganic salts.

42. An adjuvant according to claims 40, wherein the salt is selected from organic salts.

43. An adjuvant according to claims 40-41, wherein the salt is selected from salts formed with oxides, peroxides, hydroxides, carbonates, phosphates, pyrophosphates, hydrogenphosphates, dihydrogenphosphates, sulphates, and/or silicates,
and hydrates thereof.

44. An adjuvant according to claims 40-41, and 43, wherein the salt is selected from salts formed between Mg, Ca, Ba, Ti or Zr, and oxide, peroxide, hydroxide, and/or carbonate, and hydrates thereof.

45. An adjuvant according to claims 40-41, and 43-44 wherein the salt is selected from salts formed between

magnesium and oxide, peroxide, hydroxide, and/or carbonate,
calcium and oxide, peroxide, hydroxide, and/or carbonate,
barium and oxide, peroxide, hydroxide, and/or carbonate,

EP 2 368 568 A1

titanium and oxide, peroxide, hydroxide, and/or carbonate, and
zirconium and oxide, peroxide, hydroxide, and/or carbonate,
and hydrates thereof.

46. An adjuvant according to claims 40-41, and 43-45 wherein the salt is selected from magnesium hydroxide, magnesium carbonate hydroxide pentahydrate, titanium dioxide, calcium carbonate, barium hydroxide, barium peroxide, barium carbonate, barium sulphate, calcium sulphate, tricalcium silicate, calcium pyrophosphate, calcium peroxide, calcium hydroxide, tricalcium phosphate, calcium hydrogenphosphate, calcium dihydrogenphosphate, calcium sulphate dihydrate, magnesium carbonate, magnesium sulphate, trimagnesium phosphate, magnesium silicate, magnesium trisilicate, titantium disulphate, zirconium sulphate, strontium peroxide, and strontium carbonate.

47. An adjuvant according to claims 40-41, and 43-46, wherein the salt is selected from magnesium hydroxide, magnesium carbonate hydroxide pentahydrate, and titanium dioxide, or the salt is selected from a combination of magnesium hydroxide and magnesium carbonate hydroxide pentahydrate, magnesium hydroxide and titanium dioxide, magnesium carbonate hydroxide pentahydrate and titanium dioxide, or magnesium hydroxide, magnesium carbonate hydroxide pentahydrate, and titanium dioxide.

48. Use of an adjuvant according to claims 40-47 or an adjuvant composition according to claims 21-39 as a component of a parenteral vaccine formulation.

EP 3 956 356 B1

49. Use of a salt formed with a Group 2 element of the Periodic Table selected from Mg, Ca, Sr, Ba and Ra, or a Group 4 element of the Periodic Table selected from Ti, Zr, Hf, and Rf,
and hydrates thereof,
as an adjuvant in a vaccine formulation for parenteral administration,
with the proviso that the salt is not calcium phosphate, is not magnesium hydroxide in combination with aluminium hydroxide or aluminium oxide and is not calcium hydroxide in gel combination with zinc hydroxide, lecithin and polyalphaolefine.

50. Use of a salt formed with a Group 2 element of the Periodic Table selected from Mg, Ca, Sr, Ba and Ra, or a Group 4 element of the Periodic Table selected from Ti, Zr, Hf, and Rf,
and hydrates thereof,
as a component of an adjuvant composition,
with the proviso that the salt is not calcium phosphate, is not magnesium hydroxide in combination with aluminium hydroxide or aluminium oxide and is not calcium hydroxide in gel combination with zinc hydroxide, lecithin and polyalphaolefine.

51. Use according to claims 49-50, wherein the salt is selected from inorganic salts.

52. Use according to claims 49-50, wherein the salt is selected from organic salts.

53. Use according to claims 49-51, wherein the salt is selected from salts formed with oxides, peroxides, hydroxides, carbonates, phosphates, pyrophosphates,

EP 0 968 726 A2

hydrogenphosphates, dihydrogenphosphates, sulphates, and/or silicates,
and hydrates thereof.

54. Use according to claims 49-51, and 53 wherein the salt is selected from salts formed between Mg, Ca, Ba, Ti, or Zr, and oxide, peroxide, hydroxide, and/or carbonate,
and hydrates thereof.

55. Use according to claims 49-51, and 53-54, wherein the salt is selected from salts formed between

magnesium and oxide, peroxide, hydroxide, and/or carbonate,
calcium and oxide, peroxide, hydroxide, and/or carbonate,
barium and oxide, peroxide, hydroxide, and/or carbonate,
titanium and oxide, peroxide, hydroxide, and/or carbonate, and
zirconium and oxide, peroxide, hydroxide, and/or carbonate,
and hydrates thereof.

56. Use according to claims 49-51, and 53-55, wherein the salt is selected from magnesium hydroxide, magnesium carbonate hydroxide pentahydrate, titanium dioxide, calcium carbonate, barium hydroxide, barium peroxide, barium carbonate, barium sulphate, beryllium oxide, calcium sulphate, calcium silicate, dicalcium silicate, tricalcium silicate, calcium pyrophosphate, calcium peroxide, calcium hydroxide, tricalcium phosphate, calcium hydrogenphosphate, calcium dihydrogenphosphate, calcium sulphate dihydrate, magnesium carbonate, magnesium oxide, magnesium dioxide, magnesium sulphate, trimagnesium phosphate, magnesium silicate, dimagnesium

trisilicate, magnesium trisilicate, titantium disulphate, zirconium dioxide, zirconium hydroxide, zirconium sulphate, strontium peroxide, and strontium carbonate.

57. Use according to claims 49-51, and 53-56 wherein the salt is selected from magnesium hydroxide, magnesium carbonate hydroxide pentahydrate, and titanium dioxide, or wherein the salt is selected from a combination of magnesium hydroxide and magnesium carbonate hydroxide pentahydrate, magnesium hydroxide and titanium dioxide, magnesium carbonate hydroxide pentahydrate and titanium dioxide, or magnesium hydroxide, magnesium carbonate hydroxide pentahydrate, and titanium dioxide.

58. A method of generating an immune response in a subject comprising administering to the subject a parenteral vaccine formulation according to claims 1-20.

59. Vaccination or treatment of a vertebrate including a human being comprising administering a vaccine formulation according to claims 1-20.

60. A process for preparing a parenteral vaccine formulation according to claims 1-20 comprising adding liquid to a dry form of or a pre-formed gel of the salt formed with a Group 2 element of the Periodic Table selected from Mg, Ca, Sr, Ba and Ra, or a Group 4 element of the Periodic Table selected from Ti, Zr, Hf, and Rf, the salt not being calcium phosphate, not being magnesium hydroxide in combination with aluminium hydroxide or aluminium oxide and not being calcium hydroxide in gel combination with zinc hydroxide, lecithin and polyalphaolefine, thereby obtaining an adjuvant composition, and mixing said adjuvant composition with one or more immunogenic substances and optionally

EP 0 968 726 A2

pharmaceutically acceptable carriers and/or excipients, thereby obtaining the parenteral vaccine formulation.

61. Parenteral vaccine formulation obtainable by the process according to claim 60.